September 24, 2012

Sue Shallal, Ph.D.

RE: EPA's SAB Draft Report Concerning EPA's Application of Computational Toxicology (Comptox) Data in Risk Assessment.

Dear Dr. Shallal,

The American Chemistry Council (ACC) appreciates the opportunity to provide oral comments on EPA's Draft Report Concerning EPA's Application of Computational Toxicology (Comptox) Data in Risk Assessment. ACC and its members make substantial, ongoing investments in research to support product development, health, safety and environmental protection, and to abide by product stewardship and regulatory policies. We have a significant interest in EPA's Comptox outputs in risk assessment, and we have long sought to improve the quality of government science generally and risk assessment in particular.

Overall, the Draft SAB report is to be commended. It outlines many of the important areas that need to be addressed to establish scientific confidence in Comptox assays, batteries and prediction models.

In addition to the recommendations contained in the SAB report, the SAB may wish to consider addressing the following additional issues:

- The SAB should consider recommending that EPA develop explicit activities to establish the scientific confidence for computational profiling assays and prediction models that is matched up to the specific intended use. (examples for frameworks that may be applicable to establish such scientific confidence: OECD QSAR Principles and the 2010 Institute of Medicine Report on Biomarkers)
    - o In this regard, a lesser degree of confidence may be acceptable in regulatory priority setting compared to the confidence required to support hazard characterization or a classification/labelling decision. But even for priority setting, an appropriate degree of validation is needed.
- The SAB's Data Use Guidance recommendation is a critical need. It is needed not only for the assays themselves, but also for the prediction models and related tools, such as ToxPi.
    - o For example, in ToxPi, each slice of the "pie" is normalized to the highest score of the set of chemicals tested, not to a fixed, external reference set of standards. The SAB may wish to consider recommending EPA develop specific Data Use Guidance for ToxPi and that the Agency establish a fixed, external reference set of standards.

- There is a need for a transparent data quality control / quality assurance programs for the Comptox databases. For both NCCT and for NCEA. And there needs to be a process in place for errors to be brought to the attention of EPA and for corrections to be made and announced. The SAB may wish to recommend EPA develop such QA/QC procedures for each Comptox database.
- There is a need to have the actual data available for external analysis, verification of prediction models, and for development of new and improved models, etc. The SAB should commend NCCT for their openness and engagement of stakeholders in the Communities of Practice. But, such transparency varies, and does not appear to be operable in the NexGen program. Therefore, SAB should consider recommending that this openness and transparency needs to be expanded / extended to NCEA as well as NCCT.
- The dissemination of data, assay results and prediction models will also improve the degree of independent scientific peer review, enabling reviewers to independently verify modeling and predictions. The SAB may wish to make this a clear recommendation. clear

Thank you for considering our comments. Please do not hesitate to contact me (Rick_Becker@americanchemistry.com) if you have any questions.

Sincerely,

Richard A. Becker, PhD, DABT
Senior Director